nuclein, believing the effect to be due to saline solution; this we shall see is erroneous. The experimental and clinical therapeutics of nuclein begin as far back as 1892 by Löwitt, then by Vaughan in 1896, after which no one seems to have worked much with the substance until the period 1903 and 1907, during which time several articles appeared. The most noteworthy of these are three coming from the Mikulicz Clinic by Mikulicz, Miyake, and Renner. They found that by the use of yeast nuclein they could increase the resistance of experimental animals to artificial infection and could materially reduce the morbidity and mortality from postoperative peritonitis. They lay stress on the fact that they could get greater protection and greater number of leukocytes (20 to 8) by the use of nuclein than by the use of aleuronat, which they class as a mechanical attractor of leukocytes. Renner, experimenting with dosage in human beings, used 50 c.c. of a 2 per cent. solution, which means 17 mg. per kilo for a man of 70 kilo. There was usually a mild general reaction and a local puffy, sensitive swelling at the site of inoculation. Their own description of the after effects is not in harmony with their nonchalance as to the severity of the reaction. Judging by the reaction we observed in dogs, this injection must be painful. According to Renner, the reaction on the part of the leukocytes takes place anywhere from six to twenty-four hours later, and one cannot foretell when it will appear or when the effect or the decrease will be greatest. The leukocyte increase is usually pronounced, being in his highest case 452 per cent. They say that this procedure, while of distinct clinical value, is not effective against fulminating streptococcal infections.

THE INTERPRETATION OF CERTAIN BLOOD-PRESSURE RATIOS.

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During the past ten years blood-pressure determinations have apparently become an essential part of the data necessary in many instances to an understanding of conditions affecting the circulatory system. In this period much of value has been acquired from blood-pressure studies. It will be the purpose of this article to interpret certain phases of the subject, although it is realized that in the words of a contemporary, "It is not difficult for the majority of us to be beyond our depth before we know it, when we venture in these waters."[1]

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[1] McCrae, T.: Am. Jour. Med. Sc., April, 1916, in review of Sir Clifford Allbutt's Diseases of the Arteries, Including Angina Pectoris.

TYPES OF ARTERIOSCLEROSIS AND THEIR INFLUENCE UPON HYPERTENSION. From the beginning of blood-pressure determinations it has been apparent that not all types of rigid arteries were associated with hypertension. In fact, it is a matter of common observation that extreme sclerosis may exist with normal or decreased pressures. A review of the various types of arteriosclerosis may therefore be of interest at this point in an endeavor to correlate subsequently in this article various types of vascular disease with arterial pressure variations, and their clinical manifestations.

The Nodose Type of Arteriosclerosis. This is the most common form, and is characterized by whitish, flattened, and nodal thickenings of the intima. These thickenings or nodes are especially noticeable at points where smaller branches are given off from the larger arteries, such as the intercostal branches of the aorta. The aorta is, however, usually involved throughout the entire length. These nodes are the result of true hyperplasia of the connective-tissue cells of the intima, and are not the result of round-cell inflammatory infiltration. The nodes are non-vascular and may subsequently undergo localized necrosis, the so-called atheromatous ulcers, the areas of which are replaced by granulation tissue with eventual calcification and atheroma. The characteristic change is calcification and atheroma of localized patches or nodes of intimal connective-tissue overgrowth.[2] [3]

This type of arterial degeneration is not, as a rule, associated with hypertension, since the localized patches when present do not cause material contraction of the lumen of the smaller vessels.

The Senile Type of Arteriosclerosis. This type, the so-called "Moenckeberg's Sclerosis," is characterized by muscle atrophy and degeneration of the media. The muscle atrophy of the media is more important than atrophy of the elastic tissue. Compensatory overgrowth, or hypertrophy of the intima, may occur with subsequent atheroma of these areas of intimal overgrowth, or, as more frequently happens, sacculation and dilatation of the larger vessels, such as the aorta occurs, due to localized giving way of the intima. Calcification and fibrosis of the media is the essential change. This may involve the smaller vessels also, which are rigid. Savill[4] has shown in a report of 400 autopsies on individuals of an age of sixty years or over that an extensive patchy atheroma was consistent with an average longevity and absence of cardiovascular symptoms. Of course, if the patches of intimal overgrowth happen to involve the orifices of the coronary arteries the nutrition of the myocardium will suffer and will be followed by cardiac symptoms, the variety of which will depend upon the degree of obstruction. If conditions producing "hypertonus" as described by Russell[5] have been present during the time the fibrosis of the media was progressing, it is conceivable that contraction of the peripheral vessels would occur with exaltation of arterial tension. As a rule, however, the senile type of arteriosclerosis is not accompanied by marked hypertension, for while the peripheral vessels are generally rigid they are not contracted, and hypertonus appears to be lacking.

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[2] Adami, J. G.: The Nature of the Arteriosclerotic Process, Am. Jour. Med. Sc., October, 1909.

[3] Adami and McCrae: A Text-book of Pathology, 1914, p. 487.

[4] Lancet, London, 1904, p. 506.

Toxic Type of Arteriosclerosis. In this type the plaque-like nodes or patches of the intima have a translucent appearance and may resemble the nodose type, but the essential change is an inflammatory degeneration of the media. The initial nodes are more spread out and occur characteristically in groups especially in the ascending aorta and arch. These nodes are the result of a compensatory hypertrophy, but there is little tendency to calcareous change and atheroma, as in the nodose type. The toxic type of arteriosclerosis is essentially inflammatory and is seen particularly as a result of the toxins of syphilis, diphtheria, diabetes, and after lead and mercurial poisoning. The toxin of syphilis leads especially to intimal overgrowth, the nodes having a puckered appearance, with their long axis transverse to the long diameter of the vessel. In syphilis the vasavasorum of the first portion of the aorta are particularly affected, and round-cell infiltration occurs about their branches in the adventitia and media. The toxins of typhoid fever seem frequently to have an ill effect upon the intima of the peripheral arteries, the manifestations of which are to be seen in patches of overgrowth. The diphtheria toxin particularly affects the media.

In chronic degenerative diseases affecting the permeability and function of the kidneys the characteristic arterial changes of the toxic type are seen. In addition, hypertonus seems to go hand-in-hand with so-called chronic glomerulonephritis. It has been generally believed that the degenerative media changes in the arteries are brought about by the increased pressure resulting from disturbed kidney function and that ultimately contraction of the arterioles occurs.

Leonard Hill has shown that increased pressure in the larger trunks normally causes the arterioles to contract, and that the higher the pressure the more the arterioles tend to contract. It is this tendency to contraction of the lumen of the arterioles in this type of arterial degeneration which distinguishes it from the types before mentioned. The diastolic pressure is in consequence higher in this group. Allbutt[6] apparently believes in the hypertonus factor described by Russell, for he has protested against the use of the term arteriosclerosis as a disease *per se*. He believes that the arterial degenerative changes may occur as a result of any cause producing high pressures. Savill[7] and Russell[8] have been able to demonstrate an increase in the muscular coat of the smaller arteries accompanying arterial degeneration in the larger trunks. This hypertrophy, they believe, implies abnormal contraction. This is in accord with the belief of Hasebroek[9] that contraction of the arteries is an active muscular act to assist the heart in maintaining an adequate pressure for blood flow, while dilatation of the arteries is a passive result of the injected volume of blood during systole. Adami and McCrae[10] have expressed their belief as to the relationship between hypertonus and arteriosclerosis as follows: "We support the view that arteriosclerosis as such is not in general of infective origin, and indeed is not an inflammatory process. We hold that it is the expression of a disordered relationship between the internal pressure to which the artery is subjected and the strength of the arterial wall, that strength depending in the main upon the condition of the media."

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[5] Arterial Hypertonus, Sclerosis and Blood-pressure, Edinburgh, 1907.

[6] Brit. Med. Jour., October 20, 1906.

THE AUSCULTATORY METHOD OF PRESSURE DETERMINATIONS. Both systolic and diastolic pressures are best taken by auscultation, with a stethoscope of the disk type, over the brachial artery on the inner aspect of the arm below the compressing arm band. Korotkoff[11] first described this method in 1905. In applying this method, compression is made in the arm band to a point above which all sound is heard in the artery. The air-pressure is then gently released, and as the pressure falls the point at which the first sound is heard is taken as the systolic pressure. A series of similar clear sounds are then heard which are soon replaced by a series of murmurs, and a second series of clear sounds. These clear tones are shortly replaced by dull tones which rapidly disappear. Korotkoff believed that the diastolic pressure corresponded to the first dull tone following the second series of clear sounds. This is, as a rule, about 5 mm. above the point of disappearance of all sound.

Latterly, Hooker and Southworth,[12] using the Erlanger instrument in combination with the method of Einthoven and Geluk for recording brachial sounds, have expressed the opinion that for clinical purposes the point of cessation of sounds in the artery corresponds with the diastolic pressure. I have taken the dull tone following the second series of clear sounds as indicative of the diastolic pressure, but am inclined to believe, with further experience, that in the majority of cases of rapid heart action this transition is exceedingly difficult to determine. It would undoubtedly simplify the procedure if the point of disappearance of pulse sound was taken as the diastolic pressure. Further experience will probably show the wisdom of adopting this point, since for all practical accuracy it answers the purpose.

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[7] Tr. Path. Soc. of London, vol. lv.

[8] Loc. cit.

[9] Deutsch. Arch. f. klin. Med., 1911, cii, 567.

[10] Loc. cit.

[11] Mitt. d. k. mil. med. Akad. zu St. Petersburg, 1905, xi, 365.

[12] Arch. Int. Med., 1914, xiii, 384.

THE SYSTOLIC PRESSURE. For nearly a decade after the estimation of blood-pressure became a matter of clinical interest, attention was largely directed to the systolic pressure. The literature to about 1910 in fact mentioned but rarely any other than the systolic pressure. The usual method was to determine the point of palpatory obliteration of the pulse wave distal to the compressing arm band. The auscultatory method has, however, greatly simplified the accuracy of blood-pressure readings, and has gradually supplanted the palpatory method. The systolic pressure may be defined as the sum total of pressures existing in the artery under observation during cardiac systole. It is made up of the diastolic pressure existing in the artery during the cardiac pause or diastole plus the pressure or force exerted by the contracting ventricle in excess of the diastolic pressure. This latter, known as the pulse-pressure, represents the expenditure of force necessary to move the column of blood in the artery. It represents motion through the expenditure of kinetic energy. During systole, as the intraventricular pressure rises, the aortic valves do not open until the pressure at least equals the pressure then existing in the aorta, *i. e.*, the diastolic pressure. The ultimate or total pressure reached must be considerably in excess of the diastolic pressure, for if such a result were not attained at the end of systole there would be no pressure effective to promote blood movement. The pulse-pressure then represents the effective *vis-a-tergo* promoting blood movement. The pressure exerted by the cardiac systole up to the moment of opening the aorta valves avails the circulation nothing at all. It is, so to speak, kinetic energy wasted in overcoming static or potential energy. It is therefore the sum of the diastolic and pulse-pressures which go to make up what has been recognized as the systolic pressure.

The systolic pressure represents the total expenditure of kinetic energy on the part of the myocardium necessary to effect blood movement at a given moment. It represents heart work and is relatively a variable force, since the circulatory requirements may have considerable variation, dependent upon emotions, such as anger or anxiety, apprehension and nervous unrest, and upon physical stress and exertion, which may for the time being draw upon the cardiac reserve strength. It is a much more variable pressure than the diastolic pressure. An increased systolic pressure from this point of view means an increased cardiac expenditure of energy and nothing more, while a decreased pressure represents less expenditure of cardiac energy. The height of the systolic pressure in a compensated heart is dependent upon the height of the diastolic pressure (*i. e.*, the arterial tonus) to a large degree. But an increased systolic pressure may also depend upon certain factors, such as liver cirrhosis, mediastinal growths, pleuritic effusions, aortic aneurysm or incompetent heart valves, not necessarily associated with arterial hypertonus, but making necessary the expenditure of extra force in an endeavor to promote circulatory equilibrium.

THE DIASTOLIC PRESSURE. The diastolic pressure represents the more or less constant potential or static pressure existing in the artery under observation during the diastolic pause between succeeding systoles. The chief factor affecting this pressure is the tonus and degree of elasticity of the arterial wall. Of probably less importance is blood volume and viscosity. The following distinction may be made that while the total or systolic pressure represents cardiac force the diastolic pressure represents the resistance offered by arterial tonus. The diastolic pressure consequently should be taken as the index of arterial tension. A high diastolic pressure therefore means hypertension irrespective of the height of the systolic pressure, and *vice versa* a lowered diastolic pressure means hypotension, irrespective of the systolic pressure.

In an examination of over 500 individuals, for the most part below the age of forty years, who presented no symptoms of circulatory disease, I have found that the average diastolic pressure was between 80 and 85 mm. Hg. A persistent diastolic pressure of 100 signifies, in my experience, a mild degree of arterial hypertonus. If this pressure persistently averages 110 a more definite hypertonicity is present and usually signifies the beginning of an advancing vascular disease with contracted arteries. If a diastolic pressure of 115 to 130 is maintained persistently, definite vascular contraction has occurred. To this there are few exceptions. There have been occasional instances in which arterial hypertonicity of a temporary duration has occurred, due to toxemia, the result of a temporary hyperglycemia, or urea retention (as in acute nephritis). In these instances of temporary duration the diastolic pressure has fallen as the cause has been relieved.

When the diastolic pressure is maintained at a high level, from 130 to 160, the conditions are present which have so long been associated with contracted kidneys. The associated kidney disturbance is but an evidence of the vascular changes, the hypertonus and constriction, present throughout the circulatory tree. It does not follow nor has it been proved that the primary cause of the hypertonus is the result of altered kidney function. The kidney damage is probably coincidental to the vascular damage inflicted elsewhere through metabolic factors many times unknown, producing hypertonicity and constriction of the arteries. The essential point is that the diastolic pressure is the true index of arterial tension.

THE PRESSURE-RATIO.[13] With a heart possessing normal contractility and tonicity, so far as one may judge in the present state of knowledge, there exists within certain limits a normal ratio between the diastolic and pulse-pressure. As has been before mentioned it is the sum of these pressures which make up the total or systolic pressure, so for practical purposes the systolic may for the time being be disregarded. In a study of about 500 individuals with supposedly normal hearts I have noted that the pulse-pressure averaged about 50 per cent. of the diastolic pressure. That is, with a diastolic pressure of 80 mm. the pulse-pressure was an additional 40 mm.; with a diastolic of 82 mm. the pulse-pressure was 41 or 42 mm.; while with a diastolic of 90 mm. the pulse-pressure was 45 mm. The normal pressure-ratio was therefore formulated as follows:

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[13] In earlier papers dealing with this subject the term heart-load was used to designate the increased ratio between pulse-pressure and diastolic pressure found in the cardiac groups. Such a term while suitable for the cardiac groups is inadequate for the cerebrorenal group of hypertension, for while the ratio between pressures is usually within normal limits in this group when the heart is compensated, the heart-load or work is necessarily increased because the heart is contracting against an increased diastolic pressure. The term pressure-ratio is therefore to be preferred.

THE PULSE-PRESSURE DIVIDED BY DIASTOLIC PRESSURE or $\frac{\text{P. P.}}{\text{D. P.}}$

The ratio here given merely expresses the fact that under normal conditions, as well as in certain abnormal states in which the heart is in compensation, a pulse-pressure force 50 per cent. in excess of the diastolic pressure is required by the heart in systole before the aortic valves open and mass movement of blood is affected toward the periphery. The ratio also expresses the relationship between the kinetic energy expended by the cardiac contraction in moving the blood column and the potential energy or resistance offered by the arterial walls and volume of blood which they contain. This ratio may vary within normal limits between 40 and 60 per cent. The tendency toward this ratio is always evident with compensating hearts in pathological states with true hypertension due to an increased diastolic pressure (*vide infra*). In such cases, as the diastolic pressure increases due to vascular contraction and rigidity representing a true obstruction to cardiac output, the pulse-pressure increases, due to the expenditure of increased cardiac force in the endeavor to adequately supply the periphery with blood. The systolic pressure is consequently increased when the diastolic pressure is high if the heart is compensating for the increased circulatory load it is obliged to carry.

Strassburger[14] first attempted in 1905 to obtain a pressure-ratio as a means of estimating cardiac efficiency founded upon pressure variations. His ratio was obtained by dividing the pulse-pressure by the systolic pressure.

Tigerstedt[15] has also suggested this formula for determining the efficiency of the heart as a pump. His formula takes into account the factor of blood velocity as follows:

$$\frac{\text{Pulse-pressure} \times \text{pulse-rate} = \text{velocity}}{\text{Systolic pressure} \times \text{pulse-rate} = \text{work}} = \text{heart efficiency.}$$

$$\text{This is equivalent to } \frac{\text{pulse-pressure}}{\text{systolic pressure}} \text{ or } \frac{\text{P. P.}}{\text{S. P.}}$$

This formula appears objectionable for the following reasons: When the intraventricular pressure rises during cardiac systole the aortic valves cannot open until this pressure at least equals the diastolic pressure in the aorta. The intraventricular pressure up to this point does not affect blood movement at all, it being the pressure exerted by the myocardial contraction in excess of the diastolic pressure, *i. e.*, the pulse-pressure, which is useful for the purpose of blood movement during the cardiac systole. It therefore appears that the ratio of pulse-pressure to a diastolic pressure should be taken as an expression of the measure of work done by the myocardium in overcoming peripheral resistance.

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[14] Quoted by Barach and Marks, Arch. Int. Med., 1914, xiii, 648.

[15] Quoted by Hirschfelder, Diseases of the Heart and Aorta, 1910, p. 26.

THE DIFFERENTIATION OF CERTAIN TYPES OF HYPERTENSION. In applying the formula here given to a considerable number of patients manifesting symptoms of vascular disease it became at once apparent that certain groups could be differentiated. The differentiation depended to a large degree upon the height of the diastolic pressure and the relationship which this pressure appeared to bear to the pulse-pressure.

THE CEREBRORENAL GROUP OF HYPERTENSION. In this group were found the patients with evidences of damage to the arteries in general and to the kidneys in particular. When the damage had been long sustained the diastolic pressure was persistently high, and if the heart were able to compensate for the obstruction offered by the higher diastolic pressure the systolic pressure was increased in practically normal ratio. This group comprised those patients with chronic nephritis of the so-called diffuse or interstitial variety. Polyuria was practically always present. The quantity passed at night was increased. The specific gravity was low, varying between 1.005 and 1.015. Periodically abundant casts were found and serum albumin was present. Such damaged kidneys, as is well known, have difficulty in excreting urinary solids, and the tendency to urea retention in the blood was always marked. If the protein food intake was in excess of 75 to 100 grams daily the tendency to urea retention would many times produce an aggravation of the symptoms. This tendency was evident in many patients who followed a careful diet and whose daily intake of protein would not exceed 50 grams.

The main subjective symptoms were dyspnea usually on exertion, a feeling of pressure in the head frequently referred to the back of the neck, weakness, restlessness at night and unsatisfying sleep, vertigo, early morning headache wearing off by noon, mental confusion or lack of the usual initiative and ability for concentration. Retinal and subconjunctival hemorrhages occurred in about 10 per cent. of the patients. The diastolic pressure, as before mentioned, was high, varying from 120 to 165, while if the heart was able to compensate for the obstruction offered by the increased diastolic pressure, the systolic pressure was high also. The ratio, as before expressed, between the pulse-pressure and the diastolic pressure was in an average of many readings taken in 42 cases, usually within the normal limits of 40 to 60 per cent. The average age of these patients was fifty-five years. The average systolic pressure was 200, the diastolic 132, the pulse-pressure 68, while the pressure-ratio was 51 per cent. Twenty deaths have occurred in the series of 42 patients, giving a mortality of 48 per cent. within the three years of observation. In this group of 42 patients observed over the past three years the nephritic damage appeared to be but part of the general vascular pathology. The kidney manifestations appeared to be incidental to the general changes, which may be designated under the heading of Vascular Disease. The kidney symptoms and the high diastolic pressures which accompanied secondary contraction of the kidneys appeared to be the result of unknown metabolic factors producing hypertonus and contraction of the peripheral arteries. These vessels were rigid, but they were also contracted and their lumen diminished. Such must have been the case or the diastolic pressure would not have been so persistently increased.

I have believed from earlier observations, as well as from this series of 42 cases, that the danger to such patients because of the high diastolic pressure lay more particularly in cerebral accidents such as hemorrhage or thrombosis or cerebral edema. The mode of death in the majority has convinced me that such is the case. I have therefore designated such patients under the cerebral or cerebrorenal group of hypertension, although the general term vascular disease covers the ground more adequately.

Cardiac symptoms were many times prominent features in such patients. In the majority of the patients of this group, cardiac hypertrophy had occurred as a result of increased work in pumping against the increased diastolic pressure. The laryngeal edema leading to a constant desire to cough, the dyspnea which was many times distressing, the edema of the extremities and of the base of the lungs and the gallop rhythm pointed to cardiac disturbance. Such cardiac manifestations seemed to occur because of myocardial fatigue, and in such instances the pressure-ratios showed alteration due to a decreased pulse-pressure. This resulted in a lower systolic pressure while the diastolic was less affected. This seemed to occur because of inability due to fatigue to furnish an adequate amount of pressure or force in excess of the diastolic pressure to affect normal blood movement and stasis resulted. In such instances decreased urinary output usually was present and the symptoms due to increased retention of urea in the blood occurred. When an efficient digitalis preparation was administered at the time of such symptoms two purposes were secured: (1) the heart acquired increased tonus and force, and (2) diuresis was stimulated. The systolic pressure soon approached its former normal high level and the diuresis washed out the retained urea from the blood.

A certain proportion of patients in this group, 10 per cent.

(2 out of 20), have died as the result of myocardial exhaustion, but the much larger proportion clinically suffered cerebral hemorrhage or thrombosis and edema as a part of what we have for so long considered to be uremia. Whether a cerebral or a cardiac death is more likely to occur would seem to depend to a large degree upon the localization of the vascular degeneration. The degree of degeneration does not seem to be the same throughout the arterial system. In one patient the cerebral vessels may have suffered more than the coronary. Much may depend upon the condition of the vessels from the effects of some previous disease, as syphilis or the acute infections, such as typhoid or rheumatic fever. Syphilis, as is well known, seems to have a predilection for the aorta, the aortic orifice and by contiguity the coronary orifices.

From the stand-point of pathological physiology the kidneys in this group have difficulty in excreting urea and non-protein nitrogen products of metabolism. Few of these patients die in anuria, however. There has always been evidence of some ability to excrete water unless obstruction had existed, such as an enlarged prostate or uterine fibroid pressing upon the ureters. From the anatomical stand-point thrombosis of, or hemorrhage from, the cerebral vessels frequently occurred. The two processes altered kidney function and cerebral vascular structure often appeared to go hand-in-hand.

From the stand-point of prognosis it appeared that the higher the diastolic pressure the greater was the danger of a cerebral death.

THE CARDIAC GROUP OF HYPERTENSION. The second group which was differentiated by the study of the blood-pressure ratio was the cardiac group. In this group, while the systolic pressure was in some instances as high as in those of the cerebral group, the diastolic pressure was, as a rule, but little higher than the normal. The pulse-pressure was in consequence much higher than normal and the ratio of pulse-pressure to diastolic pressure was much increased. An average of the systolic pressures in the 32 patients of this group was 178 while the diastolic average was 93. Instead, therefore, of a normal variation in the pressure-ratio of 40 to 60 per cent. the ratio was increased to 92 per cent. This increased load over the normal limits stamped the cases as cardiac. This group was largely made up of those patients manifesting cardiac symptoms without the clinical evidences of vascular disease and its associated nephritis. It comprised those with damaged valves, with aortic sclerosis, dilatation, or aneurysm, with liver cirrhosis, with gouty manifestations, with emphysema, with syphilis or an earlier history of lead poisoning, and those whose lives had been given to hard physical labor calling for unusual cardiac demands. The symptoms of nephritis were usually lacking in the patients of this group. Such albumin as was found occasionally to be present in the urine could be attributed to stasis. The symptoms, such as polyuria, the tendency to blood-urea retention, the low specific gravity, the showers of casts were conspicuous by their absence.

The main subjective symptoms were fatigue on exertion, anginoid pains in the chest, cardiac arrhythmias due to ventricular extrasystoles or auricular fibrillation, palpitation, and dyspnea. The heart was hypertrophied in about half of the cases and likewise the peripheral arteries were rigid to palpation, but *the essential feature was that the smaller arteries, although rigid and sclerotic, were much contracted or the diastolic pressure would have been increased.* The distinctive feature of this group was the low diastolic pressure as compared with the cerebrorenal group.

The increased pressure-ratio was maintained in the patients of the cardiac group with little variation, as a rule, while the heart muscle was in compensation. In fact, in many instances the early signs of decompensation were associated with a falling systolic pressure, the so-called "primary high, secondary low" sequence. Death occurred in most instances with the symptoms of a gradually failing heart muscle or, more explicity, the symptoms pointed to a cardiac death. The systolic pressure was high in this group when the heart was in compensation, because the arterial tubes were rigid and did not passively dilate during systole to accommodate the increased blood flow into them caused by the cardiac contraction.

The prognostic point of value in the cardiac group of patients seemed to be in the maintained height of the systolic pressure as an evidence on the part of the myocardium of compensation for increased work. A falling systolic pressure in the cardiac group of hypertension was of evil augery. It usually signified varying degrees of cardiac dilatation.

On the whole the prognosis was better in this group than in the preceding cerebrorenal group, with much higher diastolic pressures. Of the 32 patients,.of an average age of sixty-two years, 8 have died within three years of observation, giving a mortality of 25 per cent. All have died a clinical cardiac death with one exception, in which the death may have been cerebral and in which autopsy was not permitted. In the patients of the cerebrorenal group there was not only the danger of cerebral hemorrhage, or of cerebral thrombosis and edema incident to the development of uremia, but also the possible danger of cardiac failure which occurred in about 10 per cent. of the deaths in that group. In the cardiac group the danger appeared to be entirely cardiac and the deaths which occurred, with possibly one exception, were due to gradual myocardial exhaustion or, more acutely, with dilatation and pulmonary edema, or to angina pectoris. The patients of the cardiac group appeared to be better risks for anesthesia by ether or by nitrous oxide-oxygen than those of the cerebrorenal group with high diastolic pressures.

THE PRESSURE-RATIO IN ANGINA PECTORIS. In angina pectoris so much apparently depends upon the patency of the coronary orifices and the rigidity or absence of thrombotic obstruction to the coronary arteries, as well as the condition of the root and the first portion of the aorta, that little might be expected from a diagnostic stand-point from the study of blood-pressure variations. I have at hand repeated observations covering 15 patients studied during the past six years; 8 are living and 7 have died in an attack. The average age of the living is now fifty-nine years, the average age of the seven who died was sixty-one years at death. There were 9 males and 6 females. The average systolic pressure of 14 of these patients was 179 and the average diastolic pressure 100. The pressure-ratio average was 80 per cent. The highest systolic pressure observed was 250 while the highest diastolic pressure was 140. The lowest systolic pressure was 115 and the lowest diastolic pressure was 40, which occurred in a patient with aortitis and dilatation with relative aortic regurgitation from stretching of the aortic ring. The average age of the 9 males at the time of their first attack was fifty-eight years, while the average age of the 6 females at the time of their first attack was sixty years. The youngest patient was forty-two at the time of his first attack while the oldest was seventy-three. Two of the patients, 1 male and 1 female, died suddenly during their attack from rupture of the posterior wall of the left ventricle into the pericardium. The walls of the ventricles showed evidences of an earlier hemorrhagic infarction about the points of rupture. Osler in the Lumleian Lectures of 1910 before the Royal College of Physicians mentioned one patient in whom the systolic pressure rose to 340 mm. during an attack of angina. I have come to regard with relatively greater seriousness the angina patients who have normal or subnormal systolic and diastolic pressures. Those in my experience who have had exalted blood-pressures have survived the longest.

THE PRESSURE-RATIO IN CARDIAC LESIONS WITHOUT HYPERTENSION. This group comprised those patients with cardiac lesions whose systolic and diastolic pressures were not increased. It was made up of 20 patients with average systolic pressures of 118 and average diastolic pressures of 62. The pressure-ratio was therefore increased from the normal of 40 to 60 per cent. to 90 per cent. The greatest increase was found in 6 patients with aortic regurgitation. Their average systolic pressure was 140 while the average diastolic pressure was 40. The pressure-ratio was therefore greatly increased to 250 per cent. In no other chronic cardiac conditions with which I am familiar were so low diastolic pressures encountered as in aortic regurgitation. This point appeared to have diagnostic significance in the differentiation of cardiac murmurs.

In considering prognosis in cardiac lesions without hypertension from the stand-point of the pressure-ratio many instances were observed in which a greatly increased ratio appeared to be compatible with a few subjective symptoms of decompensation. This was to be expected, since the greatly increased pulse-pressure was evidence that the myocardium was able to furnish adequate force to affect blood movement in compensation for the valvular disability. When the cardiac force became inadequate as the result of dilatation due to stress or overexertion, possibly from no more apparently serious an incident than severe paroxysms of coughing in an attack of bronchitis, the pulse-pressure was decreased and the symptoms of cardiac incompentency developed. This clinically signified dilatation, and has been observed in 16 patients. There was but little change in the diastolic pressure when cardiac dilatation occurred. The most evident change was the fall in pulse-pressure which produced a lower systolic pressure. The pressure-ratio was therefore diminished, the extent of which seemed to bear a direct relationship to the degree of myocardial embarrassment. In these 16 patients the pressure-ratio at the time of such disturbance varied from 11.5 per cent. to 30 per cent. When the systolic pressure tended to approximate the diastolic pressure the danger of cardiac failure was increased, since there was apparently insufficient force during systole to much more than overcome the diastolic pressure in the aorta, with but little pulse pressure useful to the movement of blood. As a result the cardiac and respiratory centers in the medulla suffered, and at the moment when insufficient blood supply reached them the exitus occurred.

THE PRESSURE-RATIO IN MYOCARDIAL EXHAUSTION DUE TO ACUTE AND CHRONIC ILLNESSES. In an acute illness, such as pneumonia, erysipelas, septicopyemia, or the early stage of typhoid, the diastolic pressure has a tendency to fall 5 to 10 mm. below its former level, due in all probability to the relaxing effects of the absorbed toxins, either upon the arteries directly or upon the vasomotor center. This results in an increase in the pulse-pressure and the pressure-ratio, for during the early stages of an acute infection the systolic pressure is usually sustained at or near its normal height. At least this usually occurs if the heart is capable of normal response. When the stage of heart embarrassment is reached in an acute illness, either from an abnormally high rate or perhaps from exhaustion in the endeavor to maintain the increased pulse-pressure apparently necessary to supply the periphery with blood, the systolic pressure begins to fall. The pressure-ratio is in consequence decreased. This decrease has appeared to bear a definite relationship in a considerable number of instances to the other clinical evidences of cardiac exhaustion. For example, in a patient ill for about two weeks with typhoid fever the systolic pressure was 118, the diastolic 80, the pressure-ratio 48 per cent. He developed bronchopneumonia the following day and the systolic pressure was 115, the diastolic pressure 60, the pressure-ratio 92 per cent. The following day the systolic pressure was 128, the diastolic pressure 102, and the pressure-ratio had fallen to 25 per cent, which was considered a serious sign. Stimulation in the form of caffein was administered in an endeavor to produce a corresponding rise in systolic pressure. The pulse rate was at this time 140 to 160. Six hours later the systolic pressure was 80 and the diastolic had fallen to 55. One hour before death the systolic was 80 and the diastolic 50. The pressure-ratio was, of course, of less prognostic importance than the fall of the systolic and diastolic pressures.

Numerous instances of this type could be given. In some of the instances a fairly good ratio between the pressures was maintained until very near the end under the influence of strophanthin intravenously, Nativelle's digitoxin, caffein, pituitrin, or adrenalin. The subsequent fall in pressures sometimes occurred very rapidly; in fact, the advisability of administering such marked cardiovascular stimulants has been questioned seriously in my mind in such instances upon the basis that it is possible, although one may not say probable, that exhausted heart and vessel tonus might have lasted longer had not the whip been applied so vigorously near the end of the race. This much may be said: when the diastolic pressure falls the vessel tonus has diminished; if the systolic pressure is maintained at near its normal level the heart is doing increased work because of the increase in the pulse-pressure, its ability to thus perform increased work depends upon its unknown reserve strength; should the systolic pressure begin to fall approaching the diastolic pressure the outlook is bad.

I have seen only one individual recover in an acute illness in which only ten to twelve points separated the systolic and diastolic pressures. In this instance a strong man suffered a mania at about the time his convalescence appeared to be established in typhoid. The systolic pressure during a few moments of quiet was 98 and the diastolic pressure was 88. He eventually recovered. One more instance of acute infection may be cited. A patient suffering with acute gangrenous stomatitis (Vincent's angina) and septicemia had early in her illness a systolic pressure of 120 while the diastolic pressure was 80. Five days later the diastolic pressure had fallen to 60 while the systolic pressure was maintained at 120. Two days later, with a pulse-rate of 140 to 148, temperature 103° to 104° (axillary), the diastolic pressure had fallen to 40 and the systolic pressure to 105. Death occurred about twenty-four hours later. She had taken 30 c.c. of a tincture of digitalis, the strength of which had been standardized by the cat method of Hatcher and Eggleston, during four days with no demonstrable effect.

In surgical shock in individuals with supposedly strong hearts the diastolic pressure was usually low. This was evident in repeated instances, especially if severe hemorrhage had occurred. The systolic pressure was usually maintained within normal limits so long as the heart was able to sustain the greatly increased pulse-pressure, a fact in accord with the often repeated observation of Hürthle "that with a decreased peripheral resistance there is an increase in the pulse-pressure." Such increased work did not, of course mean increased output of blood moved by the heart toward the periphery, for the heart was pumping into more or less empty vessels if severe hemorrhage had occurred, or if venous stasis had resulted in the splanchnics. Its output was diminished because of lowered venous pressure on the right side of the heart while its futile work was increased until the point of exhaustion was reached when a fall in the systolic pressure occurred.

Crile in a preliminary note about twelve years ago mentioned the rise in systolic pressure which usually occurred with the onset of peritonitis. He did not refer to the diastolic pressure. In several instances which I have observed the systolic pressure was increased during the development of peritonitis and the diastolic pressure was also increased. For example, in a patient with acute miliary tuberculosis and intestinal perforation in which operation was not advised the systolic pressure was 120 and the diastolic 105 twelve hours after the perforation. Fourteen hours later the systolic pressure was 130 and the diastolic 110. Eight hours later the systolic pressure was 145 while the diastolic was 110. Sixteen hours later (four hours before death), with evidence of a rapidly failing heart and pulse-rate of 160, the systolic pressure was 98 and the diastolic pressure 85. The two pressures were approaching each other and the heart had apparently not much more force behind it in systole than was necessary to open the aortic valves against the diastolic pressure.

Peritoneal handling, incident to surgical procedure without peritonitis, has produced a rise of both the systolic and diastolic pressures in several patients. One example may be given to emphasize that such pressure changes do not necessarily mean peritonitis, for such might be suspected from leakage after certain operations. A young man with continued uncontrollable slight bleeding from a gastric ulcer had a systolic pressure of 120 and a diastolic pressure of 90. The following day gastro-enterostomy was done. The systolic pressure rose shortly thereafter to 150 and the diastolic pressure to 115. The day following the systolic pressure was 140 and the diastolic 110. His recovery from the operation was uncomplicated.

In chronic illnesses not associated with symptoms of vascular disease, which necessitated confinement to bed, such as organic diseases of the central nervous system, the systolic and diastolic pressures were usually within normal limits until the heart muscle began to fail. At such a time the systolic pressure began to fall and approached the diastolic pressure, the significance of which was not difficult to anticipate. Any marked fall in the diastolic pressure may not occur until near the end, at which time and in some instances for twenty-four hours preceding it may be difficult, if not impossible, to secure definite pressure readings.

In the chronic severe anemias, whether secondary or primary, without evidences of cardiovascular disease, the systolic pressure was lower than normal for the age, while the diastolic pressure was markedly decreased. An average of the systolic pressures of 8 primary anemia patients with red blood counts varying from 728,000 to 1,000,000 per c.mm. was 105, the average of their diastolic pressures was 52. Such lowered diastolic pressures would be expected because of the thinner blood volume and relatively empty vessels. The pressure-ratio average in these patients was increased to 102 per cent.

CONCLUSIONS. From a study of over 150 patients manifesting various degrees of vascular disease and cardiac disability certain types of blood-pressure variations have been noted. The types for the most part may be grouped under the following heads:

1. *The cerebral or cerebrorenal type of hypertension,* which comprised those patients with vascular disease in which there were evidences of damage to the arteries in general and to kidneys in particular. A cerebral death occurred in a large proportion of these patients and the unfavorable prognosis seemed to depend upon the height of the diastolic pressure. In the patients of this group the arteries were rigid as well as contracted.

2. *The cardiac type of hypertension,* which comprised those patients without evidences of vascular disease and its associated nephritis. Death usually occurred from myocardial exhaustion. The arteries were rigid, but not contracted, or the diastolic pressure would have been increased. The prognosis seemed to depend upon the ability of the heart to sustain the increased systolic pressure as a purely compensatory measure.

3. *The Cardiac Type without Hypertension but with Increased Pressure-ratio.* This group comprised valvular and myocardial lesions which necessitated increased cardiac work. The prognosis seemed to depend upon the ability to sustain an increased pressure-ratio. Death when it occurred was due to myocardial exhaustion.

4. *The Cardiac Type without Hypertension but with Decreased Pressure-ratio.* This group comprised those patients with cardiac dilatation or those in whom marked evidences of myocardial exhaustion had occurred. The prognosis seemed to depend upon the reaction of the heart to stimulative measures in the endeavor to increase the pressure-ratio.

5. In general, it may be concluded from this study that too much reliance should not be placed upon blood-pressure variations as a guide to the condition of the circulation in any particular case, for such variations are of value only when associated with all other data. Certain groups of patients may, however, be differentiated in the manner above outlined, such differentiation possessing definite diagnostic and prognostic value.